**DOCKET NO.:** ORT-1414

**Application No.: 09/833,222** 

Office Action Dated: September 26, 2003

PATENT

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

1. (Original) An isolated and purified nucleic acid molecule encoding an α2δ-4 calcium channel subunit protein, said nucleic acid molecule comprising a member selected from the group consisting of:

- (a) a nucleic acid molecule encoding a protein having at least a 95% identity to a polypeptide comprising amino acids 1 to 1090 of SEQ ID NO:10;
  - (b) a nucleic acid molecule that is complementary to the polynucleotide of (a);
- (c) a nucleic acid molecule comprising at least 15 sequential bases of the polynucleotide of (a) or (b);
- (d) a nucleic acid molecule that hybridizes under stringent conditions to the polynucleotide molecule of (a) and has at least a 95% identity to the nucleic acid encoding a polypeptide comprising amino acids 1 to 1090 of SEQ ID NO:10;
- (e) a nucleic acid molecule that encodes a splice variant of a human alpha 2 calcium channel comprising exon 1B;
- (f) a nucleic acid molecule that encodes a splice variant of a human alpha 2 calcium channel comprising exon 37B; and
- (g) a nucleic acid molecule that encodes a splice variant of a human alpha 2 calcium channel comprising exon 1B and exon 37B.
- 2. (Original) The nucleic acid molecule of claim 1 wherein the polynucleotide is RNA.
- 3. (Original) The nucleic acid molecule of claim 1 wherein the polynucleotide is DNA.

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4. (Currently Amended) The isolated and purified nucleic acid molecule of claim 1, having a nucleotide sequence of <u>SEQ ID NO:9(SEQ.ID.NO.:9)</u>.

- 5. (Original) An expression vector to express an  $\alpha 2\delta$ -4 calcium channel subunit protein in a recombinant host, wherein said vector contains a nucleic acid sequence encoding a  $\alpha 2\delta$ -4 calcium channel subunit protein.
- 6. (Original) The expression vector of claim 5 wherein the expression vector contains a nucleic acid molecule encoding an  $\alpha 2\delta$ -4 calcium channel subunit protein having at least a 95% identity to a polypeptide comprising amino acids 1 to 1090 of SEQ ID NO:10.
- 7. (Original) A recombinant host cell containing an expression vector of claim 5.
- 8. (Original) The recombinant host cell of claim 7, wherein said nucleic acid molecule has a nucleotide sequence encoding an  $\alpha 2\delta$ -4 calcium channel subunit protein having at least a 95% identity to a polypeptide comprising amino acids 1 to 1090 of SEQ ID NO:10.
- 9. (Withdrawn) A protein, in substantially pure form having at least a 95% identity with a polypeptide comprising amino acids 1-1090 of SEQ ID NO.:10.
- 10. (Withdrawn) The protein according to claim 9, having an amino acid sequence of: SEQ.ID.NO.:10.
- 11. (Withdrawn) A monospecific antibody immunologically reactive with an  $\alpha 2\delta$ -4 calcium channel subunit protein.
- 12. (Withdrawn) The antibody of Claim 11, wherein the antibody blocks activity of the  $\alpha 2\delta$ -4 calcium channel subunit protein.

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13. (Original) A method for expressing an  $\alpha 2\delta$ -4 calcium channel subunit protein in a recombinant host cell, comprising the steps of:

- (a) transferring an expression vector capable of encoding an  $\alpha 2\delta$ -4 calcium channel subunit protein into a cell; and
- (b) culturing the cells under conditions that allow expression of the  $\alpha 2\delta$ -4 calcium channel subunit protein from the expression vector.
- 14. (Withdrawn) A method for identifying compounds that alter  $\alpha 2\delta$ -4 calcium channel subunit protein activity in a cell, comprising the steps of:
- a) contacting a compound with a cell containing an  $\alpha 2\delta$ -4 calcium channel subunit, and
  - b) measuring a change in the cell in response to the contacting step.
- 15. (Withdrawn) The method of claim 14 wherein the cell contains three additional calcium channel subunits: an alpha2 subunit, a beta subunit, and a gamma subunit; and wherein the three subunits and the  $\alpha 2\delta$ -4 subunit form a calcium channel complex.
- 16. (Withdrawn) The method of claim 15 wherein the calcium channel complex is an L-type Voltage Sensitive Calcium Channel.
- 17. (Withdrawn) The method of claim 15 wherein the measuring step is measuring the influx of Ca<sup>2+</sup> into the cell.
- 18. (Withdrawn) A method comprising the steps of:
- (a) incubating a cell membrane from a cell expressing recombinant  $\alpha 2\delta$ -4 with radioactive gabapentin (GBP) and a candidate compound, wherein the membrane comprises an  $\alpha 2\delta$ -4 subunit of calcium channel and wherein the incubating step is for sufficient time to allow GBP binding to the  $\alpha 2\delta$ -4 subunit of calcium channels in the cell membranes,
  - (b) separating the cell membranes from unbound radioactive GBP,
  - (c) measuring binding of the radioactive GBP to the cell membranes, and Page 4 of 7

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(d) identifying a compound that inhibits GBP binding by a reduction of the amount of radioactive GBP in step (c) to an established control.

- 19. (Withdrawn) A method for identifying compounds that alters  $\alpha 2\delta$ -4 calcium channel subunit protein activity, comprising the steps of:
- (a) combining a compound, a measurably labeled ligand for the  $\alpha 2\delta$ -4 calcium channel subunit protein, and a  $\alpha 2\delta$ -4 calcium channel subunit protein, and
- (b) measuring binding of the compound to the subunit protein by a reduction in the amount labeled ligand binding to the  $\alpha 2\delta$ -4 calcium channel subunit protein.
- 20. (Withdrawn) A compound active in any one of the methods of Claim 14, Claim 18, or Claim 19, wherein said compound is an agonist or antagonist of an  $\alpha$ 2 $\delta$ -4 calcium channel.
- 21. (Withdrawn) A compound active in the method of Claim 14, wherein said compound is a modulator of expression of a  $\alpha 2\delta$ -4 calcium channel subunit.
- 22. (Withdrawn) A pharmaceutical composition comprising a compound active in the method of Claim 14, wherein said compound is a modulator of calcium channel activity.